Study of M2 polarization in mouse brain

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ABSTRACT

Microglia are the resident immunocompetent cells of the central nervous system (CNS), which immediately react to any neurological insult to remove the damaging stimulus and restore tissue homeostasis. Similarly to peripheral macrophages, infective stimuli induce these cells to undergo a classical proinflammatory response (M1 activation), characterized by the production of inflammatory mediators, while in response to IL-4/IL-13 an "alternative" activation state is induced (M2 polarization), which is associated with the expression of anti-inflammatory molecules that lead to tissue repair and reconstruction.

Several studies suggest the existence of heterogeneous populations of microglia in different areas of the brain, with differences reported in cell density and morphology, proliferation rate, expression of immunoregolatory proteins and in response to TNF-α. The region-specific difference in microglial phenotypes has been ascribed to microenvoirmental signals and is suggestive of specific microglial functions. Since several CNS diseases involve specific brain regions, the region-specific reactivity of microglia could play a key role in preventing or potentiating disease progression. The aim of this study was thus to evaluate whether microglia show a region-specific M2 response. We induced M2 polarization *in vivo* by injecting IL-4 in the cerebroventricular space (icv), using different IL-4 concentrations and length of treatments. Through realtime-PCR, Western blot and immunohistochemistry analyses we evaluated the expression of M2 markers, such as Arg1, Fizz-1 and YM-1 in different brain areas. Our preliminary results show that our icv IL-4 model provides a novel and reliable manner to study M2 activation in brain; more importantly, our data show that the expression profile of M2 markers in glial cells might be region-specific. These results suggest that glial populations residing in different cerebral areas undergo specific M2 responses, with interesting consequences on the role of microglia in neurodegenerative diseases.